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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/868,120 | 06/14/2001 | David Thomas Dudley | 5968-01-SMH | 5646 |

7590 06/19/2002
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EXAMINER

HUI, SAN MING R

ART UNIT PAPER NUMBER

1617

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/868,120

Applicant(s)

DUDLEY ET AL.

Examiner

San-ming Hui

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Art Unit: 1617

DETAILED ACTION

Claim Objections

Claims 6, 14, 15, and 16 are objected to because of the following informalities: the use of parenthesis in claim 1, line 16 in page 83: "(cycloalkyl optionally containing ... N alkyl)"; in claims 14-16, parenthesis is used after every chemical name recited is considered improper. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "(PD_____)" in claim 14 renders the claim indefinite because the term is not understood.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Mynott et al. (WO 96/00082 provided in the International Search Report).

Mynott et al. teaches bromelain, a MEK inhibitor, is useful in a method of treating rheumatoid arthritis (See page 7, line 17- page 8, line 25; also, page 11, line 21-27; and claims 14-15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyazawa et al. (The Journal of Biological Chemistry, 1998; 273(38): 24832-24838 from the International Search Report), Jackson et al. (The Journal of Pharmacology and Experimental Therapeutics, 1998; 284(2): 687-692 from the International Search Report), Henry et al. (Bioorganic & Medicinal Chemistry Letters, 1998; 8(23): 3335-3340

from the International Search Report), and McGilvray et al. (The Journal of Biological Chemistry, 1997; 272(15): 10287-10294) in view of Bridges (WO 98/37881 from the International Search Report).

Miyazawa et al. teaches that MEK is critically involved in interleukin-6 synthesis by Human fibroblast-like synoviocytes (FLSs), which exhibit inflammatory cells characteristic (See page 24832, col. 1, the abstract and the first paragraph). Miyazawa et al. also teaches that MEK inhibitor can block the activation of MEK and suppression the interleukin-6 production and TNF- α (See page 24837, col. 1, first paragraph and col. 2, second paragraph). Miyazawa et al. also teaches antagonizing interleukin-6 and TNF would be effective in treating rheumatoid arthritis (See particularly page 24837, col. 1, second paragraph). Miyazawa et al also suggests that the inhibitors of MEK would be beneficial as rheumatoid therapy (See particularly page 24837, col. 2, last paragraph).

Jackson et al. teaches inhibition of MEK by a specific MEK inhibitor, SB220025, reducing both interleukin-1 β and TNF expression and SB220025 being useful in method of treating chronic inflammation (See the abstract, also page 687; both columns; also page 690, col. 2, second paragraph; particularly page 691, col. 2, last paragraph).

Henry et al. teaches that pro-inflammatory cytokines such as TNF- α and interleukin-1- β play important role in inflammatory diseases such as rheumatoid arthritis (See particularly page 3335, first paragraph). Henry et al. also teaches that inhibition of MEK can inhibit TNF- α release and thereby beneficial to rheumatoid arthritis treatment (See page 3335, first paragraph and page 3339, last paragraph).

McGilvray et al. teaches the involvement of MAP kinase (MEK) pathway in the activation of monocytic cells during transmigration to inflammatory sites (See the abstract). McGilvray et al. teaches the selective inhibition of MAP kinase by MEK-1 inhibitor, PD98059, being useful for blocking and interrupting the adhesion and recruitments of human monocytes and thereby modulating the inflammatory response (See the abstract and page 10287, col. 2, second paragraph).

The primary references do not expressly teach the active compounds herein to be MEK inhibitors useful for the treatment of arthritis.

Bridges teaches that the active compounds herein are MEK inhibitors (See page 3, line 16 – page 22, line 29).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis.

One of ordinary skill in the art would have been motivated to employ the MEK inhibitors of Bridges to treat arthritis such as osteoarthritis and rheumatoid arthritis: the activation of MEK is known to be involved in inflammatory process, such as migration and recruitments of monocytes to the inflammatory sites, in the body. Furthermore, the inhibition of MEK is known to 1) suppress the expression and release of pro-inflammatory cytokines such as interleukin-1 β , TNF- α , and interleukin-6; and 2) block and interrupt the adhesion of monocytes to the inflammatory sites. Possessing the teachings of the prior art the skilled artisan would therefore employ any known MEK

inhibitors, including those MEK inhibitors of Bridges, to treat arthritis such as rheumatoid arthritis and osteoarthritis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
June 17, 2002


RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200